Bacteremia in children: a 2-year review of experience with a pediatric blood culture protocol using BacT/Alert standard bottles

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In 84% of cases the magnitude of bacteremia in children is >5 CFU/mL [1] and a small volume of blood (1–3 mL) appears to be sufficient for blood culture in this age group [2–4]. Here, we report our experience in sepsis-risk children in evaluating the clinical usefulness of a pediatric blood culture method based on a blood/broth ratio of 1:41 and a continuously monitoring blood culture system—BacT/Alert (Organon Teknika Corp., Durham, NC, USA). The BacT/Alert blood culture set consisted of aerobic and anaerobic standard bottles (40 mL of culture medium in each case). Blood samples were obtained from children by the pediatric junior medical staff using standard aseptic technique: 1 mL of blood was distributed by needle and syringe to each bottle in the BacT/Alert standard blood culture set. The aerobic bottle was vented before loading in the BacT/Alert system to equalize the internal pressure: the other remained anaerobic. These bottles were incubated at 35 °C for 7 days under continuous shaking and monitoring conditions. Blood cultures drawn after 5 PM were kept at room temperature until 7 AM the next morning. Gram stains were made on smears from positive bottles and subcultures were made on appropriate agar plates. Isolates were identified and tested for antibiotic susceptibility by standard methods [5].

Between September 1992 and October 1994, sepsis-risk patients with BacT/Alert standard blood culture sets were enrolled in the study. Blood specimens from patients receiving systemic antimicrobial treatment and promptly incubated were included in an 'early entry-on therapy' group (EON). Blood culture sets collected more than 8 h before incubation in which the antibiotic coverage was lacking were recorded in a 'delayed entry-off therapy' group (DEOFF). The blood culture sets from patients not receiving systemic antimicrobial chemotherapy and that had been promptly incubated were recorded in 'early entry-off therapy' group (EOFF). The blood culture sets not included in the above mentioned groups were not considered for this study. Sepsis was defined according to the terms and definition proposed by the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference [6]. The clinical signs and laboratory test results included fever, leukocytosis, neutropenia, elevated ratio of immature to total neutrophils (I/T ratio), apneic and bradycardic episodes, feeding intolerance, and increased oxygen requirements. In addition, if the child responded to the appropriate antibiotic therapy the diagnosis of sepsis was considered confirmed.

The relevance (cause of sepsis or contaminant) of a microorganism isolated was based on the number of times it was recovered from multiple blood cultures, the clinical signs in the patient, and the response of the patient to antimicrobial therapy. A contaminant was defined as an isolate that was recovered from a culture of the blood but was not deemed responsible for the clinical signs and symptoms that prompted the blood culture. Data were retrieved from a database (Access 2.0 Microsoft). All analysis was performed with statistical software packages (StatView 4.1 Abacus Concepts Inc., Berkeley, CA). Parametric data were compared by the use of ANOVA. A relationship between two nominal variables was investigated by means of contingency table analyses. A probability of <0.01 was considered significant.

During the period, 2582 blood culture sets which met the protocol's criteria were included in the study. These specimens were obtained from 1010 children (479 female and 531 male), median age 2.7 months (range 0–143). A positive blood culture was found in 410 of the 2582 (15.9%) specimens that were cultured. False-positive results occurred in 21 (0.8%); for 20 of these 21, the detection time was greater than 5 days. Routine terminal subculture of negative blood culture sets was carried out on the first 617 sets; no false negatives were detected. Positive cultures were more common in those aged 0–34 months (285 observed versus 234 expected) and lower in those more than 34 months (119 versus 170) (Fisher's exact test; $p<0.0001$). In the 'DEOFF' group, comprising 763 blood culture sets (26.6% of total), a positive blood culture was found in 136 (17.8%), with a mean detection time of 29.2 h (95% confidence interval 21.2–37.1); the 'EON' group was made up of 796 blood culture sets (30.8% of total) and a positive blood culture was found in 116 (14.6%), with a mean detection time of 37.0 h (95% confidence interval 29.0–45.0). Finally, the 'EOFF' group comprised 1023 blood culture sets with 158 positive blood cultures (15.4%) and the mean detection time was 28.1 h (95% confidence interval 23.3–32.8). The effects of different conditions before processing were studied, and no significant difference was described for the rate of positive blood culture

Table 1 Summary table of blood culture results

	Observed frequencies (no. of cultures)			Expected values (no. of cultures)			Post hoc cell contributions		
	EOFF	DEOFF	EON	EOFF	DEOFF	EON	EOFF	DEOFF	EON
Positive	158	136	116	162.4	121.2	126.4	−0.5	1.8	−1.2
Negative	865	627	680	860.6	641.8	669.6	0.5	−1.8	1.2
Pathogens	71	87	94	97.1	83.6	71.3	−5.4	0.7	5.1
Contaminants	87	49	22	60.9	52.4	44.7	5.4	−0.7	−5.1

EOFF: promptly incubated, no antimicrobial chemotherapy.
DEOFF: collected more than 8 h before incubation, no antimicrobial chemotherapy.
EON: promptly incubated and on antimicrobial chemotherapy.

(chi-square; $p=0.1899$) (Table 1) and for the time to positivity detection (ANOVA; $p=0.8297$). Of 410 positive blood cultures, 252 (8.8% of all submitted cultures) were deemed clinically significant (152 episodes of sepsis from 98 patients). Contaminated blood cultures were found in 158 sets (6.1% of all submitted cultures). As shown in Table 1, the 'EON' group had a higher number of pathogens and the 'EOFF' group a higher number of contaminants (chi-square; $p<0.0001$). The microorganisms causing sepsis are shown in Figure 1. As shown in Figure 2, the pathogens' mean positivity time was 19.1 h (95% confidence interval 14.3–23.8); in contrast, the contaminants' mean time to positivity was 43.5 h (95% confidence interval 24.0–63.0) (ANOVA; $p=0.0056$).

All of the clinically important organisms were detected within 24 h. Most of the children included in the study came from neonatal intensive care unit and surgery wards; this explains the high positivity rate of blood cultures (15.9%), and also the fact that coagulase-negative staphylococci were common clinically significant isolates, particularly *Staphylococcus epidermidis*. In the 'DEOFF' group, where there had been a substantial delay in processing, we did not detect any significant difference from the groups containing cultures incubated promptly. This feature is of primary importance when blood cultures have to be processed in a laboratory with 8–10-h technologist cover. In the 'EON' group, which included patients suspected of being septic, and receiving antibiotics as prophylaxis, we did not observe

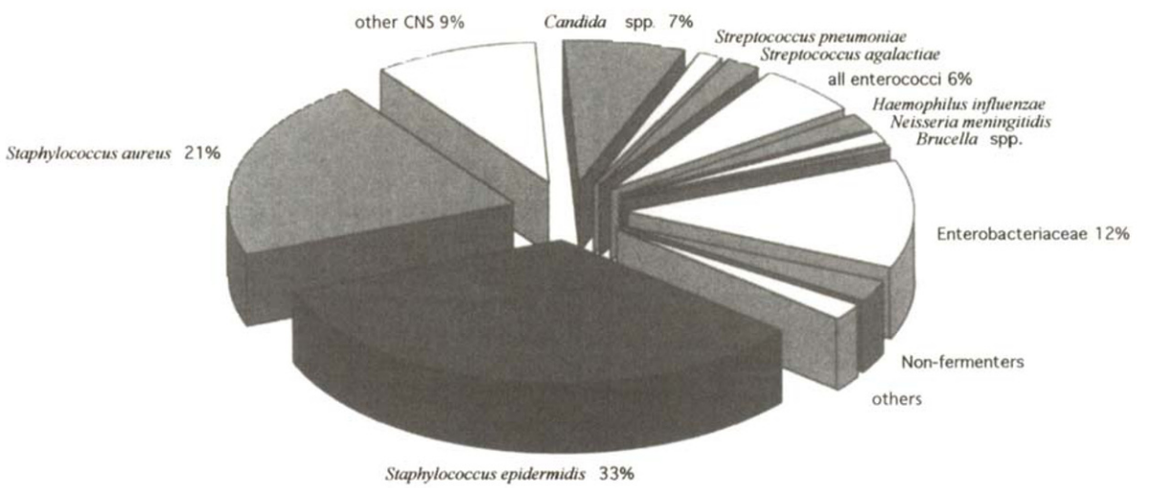

Figure 1 Distribution of organisms causing 152 episodes of sepsis in 98 children. CNS, coagulase-negatgive staphylococci. 'Others' group includes one viridans group streptococcus, one *Bacteroides fragilis*, one mixed Gram-negative rods and Gram-positive cocci.

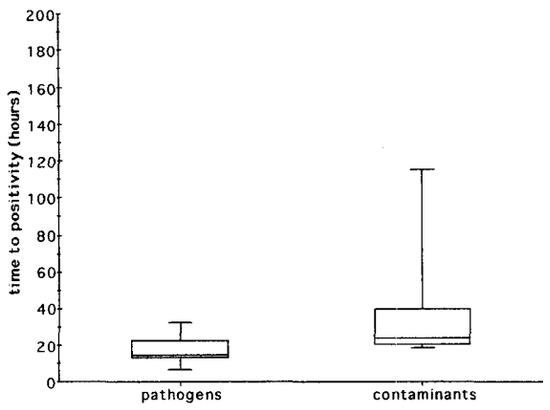

Figure 2 Box plot of mean positivity time for pathogens and contaminants (95% confidence band about median).

a fall in the yield of organisms; in fact, this group had the largest number of clinically significant positive cultures. Our protocol, using as small a blood volume as 1 mL and a dilution factor of 1:41, appears to be a valid choice to demonstrate bloodstream infection in patients under 34 months of age.

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Activity of eight fluoroquinolones against enterococci

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The incidence of nosocomial infections caused by *Enterococcus* spp. has increased dramatically in recent years. In fact, *Enterococcus* spp. are currently among the leading causes of nosocomial infection [1]. The emergence of enterococci resistant to glycopeptides, the increase in high-level resistance of aminoglycosides, the production of β-lactamase by certain strains and the intrinsic resistance of enterococci to several antimicrobials serve to limit the therapeutic options for the treatment of infections caused by these microorganisms [2].

Commercially available fluoroquinolones are not very useful for the treatment of infections caused by enterococci [3]. In recent years, new fluoroquinolones have been developed offering a broader spectrum and higher activity against Gram-positive cocci. The purpose of this study is to evaluate the activity of classical and new fluoroquinolones against clinical isolates of *Enterococcus* spp.

For this study, 100 consecutively collected clinical isolates of *Enterococcus faecalis* (50) and *E. faecium* (50) were obtained from blood cultures (54), urine samples (32) and other clinical specimens (14) from different patients in the University Hospital of Seville during 1995 and 1996. All strains were identified by both standard methods [4] and the API 20 STREP (BioMérieux; France).

The minimum inhibitory concentrations (MICs) of norfloxacin (Sigma, USA), ciprofloxacin (Bayer, Germany), sparfloxacin (Sigma, USA), ofloxacin (Hoechst, Germany), levofloxacin (Roussel, France), pefloxacin (Rhone-Poulenc, France), trovafloxacin (Pfizer, USA), clinafloxacin (Parke-Davis, USA) and